(cGVHD) was 54% and 34%, respectively. Probability of OS was 62% (CI_{95}: 48.3–78.4). There was >10-fold interpatient variability in AUC_{0-6} and MPA trough (C_0). Mean PK are shown in Table 1.

Table 1. Mean pK Parameters

	IV MMF administration			MMF PO 1st sample	MMF PO 2nd sample
Mean pK values	Day +1 (SD) [N=27]	Day +7 (SD) [N=31]	Day +14 (SD) [N=32]	Day +45-100 (SD) [N=15]	Day +45-100 (SD) [N=9]
C_{max} (mg/L)	15.4 (19.71)	12.31 (7.99)$^{\Psi}$	16.54 (13.24)$^{\Psi}$	13.15 (12.04)	13.20 (8.86)
T_{max} (h)	1.87 (0.47)	1.92 (0.55)	1.75 (0.44)	1.7 (0.98)	1.33 (0.83)
C_0 (mg/L)	0.33 (0.29)*	0.68 (0.56)*	0.72 (0.62)	1.45 (1.46)	1.43 (1.37)
C_{ss} (mg/L)	5.45 (6.34)	4.73 (2.22)	6.46 (4.07)	5.38 (3.55)	6.54 (3.55)
AUC_{0-6} (mg•h/L)	32.06 (38.09)	26.82 (12.35)$^{\Psi}$	33.71 (16.86)$^{\Psi}$	26.50 (19.03)	26.70 (15.81)
CL_{ss} (L/h•kg)	1.46 (1.04)	1.40 (0.63) *	1.17 (0.63) *	2.21 (1.43)	1.46 (1.01)
V_{ss} (L/kg)	3.04 (1.91)	3.35 (1.58)$^{\lambda}$	3.00 (2.05)$^{\lambda}$	9.77 (8.93)	18.33 (35.74)
$T_{1/2}$ (h)	1.02 (0.69)	1.35 (1.01)	2.49 (6.77)	3.17 (2.63)	10.19 (18.06)

*P=0.002.
$^{\Psi}$P=0.0003.
$^{\lambda}$P=0.001

MPA steady state clearance (CL_{ss}) (cohort 1 vs 2 vs 3 = 1.65 vs 1.45 vs 0.88 L/h·kg, P = 0.0039) and volume of distribution (V_{ss}) (cohort 1 vs 2 vs 3 = 3.87 vs 3.22 vs 2.44 L/kg, P = 0.052) were higher in pts <6 yrs. There was also a trend toward higher CL_{ss} in pts receiving MA vs NMA (1.55 vs 1.15 L/h·kg, P = 0.054). There was a significant difference in most PK values on Day +7 vs Day +14: higher AUC_{0-6} & C_{max} and decreased CL_{ss} & V_{ss} on Day +14 (Table 1). These differences suggest improved mucosal healing and/or increased enterohepatic recirculation on Day +14 vs +7. Mean MPA C_{ss} in this study was significantly higher (>5 mg/L) than previously reported in other adult and pediatric AlloSCT trials (1.6–4.8 mg/L) (Nash et al, 2005; Jacobson et al 2008). This can be explained by >2-fold higher dose of MMF (~30 mg/kg q6h) compared to others (15 mg/kg q6-8h). The incidence of aGVHD and cGVHD were comparable to previous reports. These results suggest a need for more frequent (q6h) MMF dosing in pediatric AlloSCT recipients, especially those <6 years. However, the optimal MMF dose (mg/kg) and relationship between MPA exposure and risk of acute GVHD remain to be elucidated.

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HIGH BUDESONIDE BIOAVAILABILITY IN PATIENTS WITH GASTRO-INTESTINAL (GI) GRAFT VERSUS HOST DISEASE (GVHD) AND/OR *CLOSTRIDIUM DIFFICILE* INFECTION

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Background: Therapy of acute intestinal GVHD is routinely treated with immunosuppressive agents, including systemic corticosteroids. Several reports have shown responses of using "topical" therapy with budesonide for GI GVHD. Budesonide is a potent steroid with low oral bioavailability due to high first pass metabolism by CYP 3A4. In patients with Crohn's disease, bioavailability is approximately 10–20%. No data are available in hematopoeitic stem cell transplant recipients. Several reports using budesonide for the treatment of GI GVHD have noted responses in other GVHD sites, thus questioning if active absorption was occurring. As a quality measure at our center, several patients who had GI GVHD and/or *C. Difficile* were evaluated for systemic availability of budesonide.

Methods: Random plasma budesonide levels were analyzed by HPLC/Mass Spectrometry in 8 patients with a history of GI GVHD receiving Enterocort brand of budesonide.

Results: A total of 11 budesonide plasma levels were measured in 8 patients. Seven patients had active GVHD, 5 patients had active GVHD and concurrent C. Difficile infection, and 2 patients had C. Difficile without active GVHD at the time of plasma measurements. Four of the 8 levels were measured on a budesonide dose of 9 mg TID, two on 9 mg once daily, three on 6 mg TID, and two on 3 mg TID. The mean budesonide plasma level was 0.86 mcg/dl (0.08–1.5), 0.60 mcg/dl (0.09–1.1), 0.97 mcg/dl (0.2 – 1.1) and 0.65 mcg/dl (0.2–1.1) respectively. Mean budesonide levels were higher if patients were on voriconazole (1.05 mcg/dl) than on micafungin (0.47 mcg/dl). The mean budesonide bioavailability was 37% in all patients and 50% if on Voriconazole. Thus, budesonide doses ranging from 3 mg TID to 9 mg TID would represent a potency equivalent to 40–162 mg methylprednisolone/day.

Conclusion: Systemic budesonide levels were significantly elevated in patients with acute GI GVHD. Patients on voriconazole had higher plasma levels of budesonide, possibly attributable to CYP450 inhibition. The use of oral budesonide in patients with gastro-intestinal GVHD may lead to systemic absorption and subsequent additive systemic corticosteroid effects.

IMMUNE RECONSTITUTION

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THYMIC EPITHELIAL CELLS AND DENDRITIC CELLS MEDIATE THYMIC RENEWAL THROUGH CCL25 PRODUCTION

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Impaired thymopoiesis contributes to immune deficiency following hematopoeitic stem cell transplantation (HSCT). Clinical data suggest that thymic epithelial cell (TEC) damage from the preparative regimen may compromise thymic recovery. We have previously shown that TEC are critical for thymic renewal in the setting of androgen withdrawal. These UEA+ medullary TEC provide a niche for early thymic progenitor (ETP) entry and thymocyte development by increasing the production of CCL25. Following androgen withdrawal, CCL25 accelerates thymocyte development and enhances ETP entry. Blockade of this ligand completely abrogates these affects, preventing thymic renewal. We now demonstrate that cytotoxic preparative regimens may impair thymic reconstitution by damaging stroma, decreasing CCL25 availability. In this study, we examined the effects of cyclophosphamide (CY) (240 mg/kg/mouse) or total body irradiation in female mice on TEC and medullary dendritic cell (mDC) populations and CCL25 production. At ½ myeloablative dose of 750 cGy, using flow cytometry of TEC, we show that both CY and radiation significantly deplete UEA+ medullary TEC while sparing Ly51+ CD45- cells. However, the effects of these two agents differed with regards to the proportions of TEC within the Ly51+ fraction. Radiation led to an increase in fibroblasts (CD45- Ly51+ MHCII-) with a marked reduction of cortical TEC (CD45- Ly51+ MHCII+), while this TEC subset was spared following CY administration. Furthermore, mDC were decreased following radiation while unaffected by CY. After irradiation, these alterations significantly impair CCL25 production as shown by decreased mRNA production of TEC enriched preparations and thymocyte fractions (in which only mDC produce CCL25). In contrast, CCL25 production was unaffected following CY administration, consistent with the hypothesis that the spared TEC populations preserve CCL25 production. These data suggest that cytotoxic preparative regimens may impair thymic renewal by destroying TEC and mDC populations thereby reducing available CCL25, a ligand necessary and essential for thymic recovery. Furthermore, these data suggest that different preparative regimens may impair thymic recovery to varying degrees due to discrimination of injured TEC and mDC populations, and the preservation of thymic CCL25 production. Investigation of alternative preparative regimen agents may present an opportunity to improve thymic renewal following HSCT.

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HUMAN COLON CARCINOMA CELLS EXPRESSING CMVPP65 ANTIGEN: AN IN-VIVO MODEL FOR ADOPTIVE IMMUNOTHERAPY OF CMV DISEASE

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Adoptive transfer of large doses of CMV-specific T cells (CMV-CTL) can effectively prevent CMV disease in HSCT recipients. However, data regarding the relative potency of T cells (TC) specific